REMARKS

The Official Action mailed July 25, 2005, and the prior art relied upon therein have been carefully reviewed. The claims in the application remain as claims 1 and 5-19, and these claims define patentable subject matter warranting their allowance. Accordingly, the applicants hereby respectfully request favorable reconsideration and allowance.

Acknowledgement by the PTO of the receipt of applicants' papers filed under Section 119 is noted.

The PTO has objected to applicants' abstract. In deference to the Examiner's views, applicants have deleted the original Abstract and replaced it with a new abstract, taking into account the Examiner's comments.

For the record, however, applicants believe that no words in an Abstract constitute "legal phraseology" because the Abstract is not a legal document, but is instead a technical document. On the other hand, all words which appear in a legal document would constitute "legal phraseology".

Claims 1-16 (presumably what is meant is claims 1 and 5-16) have been rejected under the second paragraph of Section 112 because of the presence of the transitional language "characterized in that" appearing in main claim 1, it

being stated in the rejection that such language renders the claims confusing. The rejection is respectfully traversed.

Attention is respectfully invited to MPEP 2111.03, second paragraph, which states that a transitional phrase "characterized by" is inclusive or open-ended, thus implying that this language is acceptable transitional language. Thus, the terminology "characterized in that" does not make the claims indefinite. [1]

Nevertheless, in deference to the Examiner's views, the transitional language in claim 1 has been changed to "wherein". Such amendment is of course of a formal nature only, not any substantial amendment relating to patentability and not a "narrowing" amendment because the scope of the claims has not been reduced. No limitations have been added and none are intended.

Withdrawal of the rejection is in order and respectfully requested.

Claims 1 and 5-19 have been rejected under Section 103 as obvious from Cahen et al WO98/19151 (Cahen) in view of Hashimoto et al USP 5,972,692 (Hashimoto). This rejection is respectfully traversed.

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[1] A quick search by undersigned on October 24, 2005, in the "USPTO Patent Full-Text and Image Database" for the word "characterized" in U.S. patent claims uncovered 156,559 U.S. Patents which include at least one claim in which the word "characterized" appears.

Applicants are of course very well familiar with Cahen, as it involves the earlier work of some of the present applicants and others, and is mentioned in applicants' specification on pages 4 and 5.

According to the rejection, regarding claim 1, "Cahen *et al*. disclose a hybrid organic-semiconductor device characterized by being composed of: (i) at least one layer of a conducting semiconductor; (ii) at least one insulating layer; (iii) a multifunctional organic sensing molecule directly chemisorbed on one of its surfaces, said multifunctional organic sensing molecule having at least one functional group that binds to said surface and at least one other functional group that serves as a sensor; and (iv) two conducting pads on the top layer making electrical contact with the electrically conducting layer, such that electrical current can flow between them at a finite distance from the surface of the device (Abstract; Page 4, Line 3-13; Figures 1,2). In addition, Cahen *et al*. disclose a semiconductor device wherein: said conducting semiconductor layer is on top of one of said insulating or semi-insulating layers, said two conducting pads are on both sides on top of an upper layer which is either said conducting semiconductor layer or another of said insulating or semi-insulating layers, making electrical contact with said conducting semiconductor layer

(Fig 2A, 2B). Cahen *et al.* do not disclose a layer of single-stranded DNA or RNA directly adsorbed to an upper layer which is either said conducting semiconductor layer or another of said insulating or semi-insulating layers wherein exposure of single-stranded DNA probe to a sample containing a target DNA or RNA, under hybridization conditions, causes either a current change resulting from the hybridization process when a constant electric potential is applied between the two conducting pads or a change in the electric potential required to keep a constant current".

According to the rejection, "Hashimoto *et al.* disclose a gene detection method wherein a single-stranded nucleic acid probe having a base sequence complementary to the gene to be detected is immobilized onto the surface of an electrode, and the nucleic acid probe is reacted with the gene sample denatured to a single-stranded form, and then the nucleic acid probe is hybridized with the gene to be detected (Abstract; Col. 2, Lines 25-50; Column 14, Example 1). They disclose immobilization of single-stranded nucleic acid probes to a base plate of a semiconductor element (Col. 26, Lines 21-27; Col. 27, Line 1). They disclose a semiconductor electrode of various materials including GaAs (Col. 8, Lines 44-55). They disclose immobilization of a nucleic acid probe to an electrode through physical adsorption (Col. 9, Lines 66-67;

Col. 19, Lines 10-11). They disclose multiple examples wherein gene detection was measured by determining the oxidation-reduction current change produced by hybridization of the test sample (Col. 14, Example 1; Col. 23, Example 17; Col. 24, Example 18; Col. 30, Example 19)".

As further stated in the rejection, Cahen indeed discloses a hybrid organic-semiconductor device in which a multifunctional organic sensing molecule is directly chemisorbed on one of its surfaces, whereas the instant application discloses, basically, a similar semiconductor device in which the multifunctional organic sensing molecule is replaced by at least one single-stranded DNA probe. In both cases, namely in the device of Cahen as well as in the DNA sensor of the instant application, the chemical bonds formed between the sensing molecule adsorbed on the substrate (e.g., GaAs) and the target molecule cause a change of the electronic properties of the substrate resulting in a change in the electric current flowing through the substrate.

However, unlike the device of Cahen, in which covalent bonds are formed, the bonds formed during DNA hybridization are different, and thus the change of the electronic properties of the substrate as a result of the hybridization in the DNA sensor of the instant application, as

well as the different change in case of complete *vs.* partial hybridization of the DNA adsorbed, were unpredictable.

Since none of the prior art documents either discloses or suggests the effect of DNA on the electronic properties of the substrate, the change in the signal in the semiconductor device, as a result of the change in the DNA configuration from single-stranded DNA to double-stranded DNA after hybridization to a target DNA or RNA, is novel and non-obvious. Thus, the subject matter of the instant application should not be regarded as an adaptation of the device of Cahen for measuring DNA.

Furthermore, applicants respectfully invite the attention of the Examiner to the proposition that he might have misunderstood the invention in the sense of not having recognized the difference between the DNA electronic sensor of the instant application and **DNA electrochemical sensors** that were known at the date of the claimed priority of the instant application, one of which of the latter is disclosed by Hashimoto.

In known electrochemical sensors of the prior art, electrodes (e.g. gold electrodes) are modified with DNA double helixes and used to monitor the electrochemistry of bound redox active intercalators. The base pair stack within

double helical DNA provides an effective medium for charge transport.

In particular, Hashimoto discloses a gene detection method wherein a single stranded nucleic acid probe having a base sequence complementary to the gene to be detected is reacted with a gene sample denatured into a single stranded form, and then the nucleic acid probe hybridized with the gene is detected (Col. 2, Lines 25-29). The nucleic acid probe is immobilized onto a carrier sensitive to physical change, preferably an electrode such as carbon electrodes, noble metal electrodes and semiconductor electrodes such as GaAs (Col. 8, Lines 33-50). The detection of the double stranded DNA is performed using intercalating agents also mentioned as "double stranded nucleic acid recognizing substances". By using these agents, capable of undergoing electrochemically reversible oxidation-reduction reaction, it is possible to determine the oxidation-reduction current repetitively (Col. 4, Lines 50-53).

Contrary to such known electrochemical DNA sensor, in the electronic DNA sensor of the instant application, the electric current flows through the semiconductor substrate, e.g. GaAs, while there is no charge transport by the DNA. As explained above, the hybridization of the DNA, which is directly adsorbed on the substrate, causes a change of the

electronic properties of the substrate resulting in a change in the current flowing through the GaAs substrate, which was unpredictable, and thus surprising and non-obvious.

Even if it were obvious to modify Cahen in view of Hashimoto, contrary to applicants' position, the resultant reconstruction of Cahen would not correspond to applicants' claims.

In view of all the aforementioned, applicants believe and submit that claim 1 would not have been obvious from Cahen in view of Hashimoto, and that the rejection under 35 USC 103(a) should be withdrawn. Such is respectfully requested.

The Examiner further analyzed the rest of the claims pending in this application (claims 5-19), comparing the features of the dependent portions of these claims with the features disclosed by Cahen, and in view of Hashimoto. According to the Examiner:

(i) all the features of claims 5-8 can be found in Cahen;

(ii) Cahen does not disclose "a layer of at least one single stranded DNA probes", as disclosed in claims 9-10; however, Hashimoto discloses "immobilization of single-stranded nucleic acid probes to a base plate of a semiconductor element (Col. 26, Lines 21-27; Col. 27, Line 1)" and "immobilization of a nucleic acid probe to

an electrode through physical adsorption (Col. 9, Lines 66-67; Col. 19, Lines 10-11)";

(iii) Cahen does not disclose "single stranded DNA probes comprise a sequence complementary to a sequence of a target DNA or RNA", as disclosed in claim 11; however, Hashimoto discloses "nucleic acid probes that have a base sequence complementary to the entire or part of a target base sequence (Page 6, Lines 65-67; Page 7, Lines 1-7)";

(iv) Cahen does not disclose "multiple single stranded DNA probes comprise a sequence complementary to a mutation sequence of a gene responsible for a genetic disease or disorder", as disclosed in claims 12-13; however, Hashimoto discloses "multiple nucleic acid probes that have a base sequence complementary to the entire or part of a target base sequence of a gene causing a genetic disease (Page 7, Lines 40-45)", "employing a base plate having a grid with at least two types of nucleic probes immobilized thereon (Col. 26, Lines 55-60)" and "examining a plurality of genes on the same base plate";

(v) Cahen does not disclose "each device carrying a different DNA probe", as disclosed in claim 14; however, Hashimoto *et al.* disclose "employing a base

plate having a grid with at least two types of nucleic probes immobilized thereon (Col. 26, Lines 55-60)" and "examining a plurality of genes on the same base plate";

(vi) Cahen does not disclose "a device of the sensor array carrying a DNA probe comprising a sequence complementary to a sequence of a target DNA or RNA", as disclosed in claim 15; however, Hashimoto discloses "nucleic acid probes that have a base sequence complementary to the entire or part of a target base sequence (Page 6, Lines 65-67; Page 7, Lines 1-7)";

(vii) Cahen does not disclose "a device of the sensor array carrying a DNA probe comprising a sequence complementary to a mutation sequence of a target gene responsible for a genetic disease or disorder and at least another of said device in the array carries a control DNA probe...", as disclosed in claim 16; however, Hashimoto discloses "nucleic acid probes that have a base sequence complementary to the entire or part of a target base sequence of a gene causing a genetic disease (Page 7, Lines 40-45)", "employing a base plate having a grid with at least two types of nucleic probes immobilized thereon (Col. 26, Lines 55-60)" and

"examining a plurality of genes on the same base plate";

(viii) Cahen does not disclose "a method for the detection of a target DNA or RNA which comprises...and monitoring either the current change resulting from the hybridization process...or measuring the change in the electric potential required to keep a constant current", as disclosed in claim 17; however, Hashimoto discloses "a gene detection method wherein a single-stranded nucleic acid probe having a base sequence complementary to the gene to be detected is immobilized onto the surface of an electrode...(Abstract; Col. 2, Lines 25-50; Col. 14, Example 1)", "immobilization of single-stranded nucleic acid probes to a base plate of a semiconductor element (Col. 26, Lines 21-27; Col. 27, Line 1)", "a semiconductor electrode of various materials including GaAs (Col. 8, Lines 44-45)", "immobilization of a nucleic acid probe to an electrode through physical adsorption (Col. 9, Lines 66-67; Col. 19, Lines 10-11)" and "multiple examples wherein gene detection was measured by determining the oxidation-reduction current change produced by hybridization of the test sample (Col. 14, Example 1; Col. 23, Example 17; Col. 24, Example 18; Col. 30, Example 19)"; and

(ix) Cahen does not disclose "single stranded DNA probes comprise a sequence complementary to a sequence of a target DNA or RNA", as disclosed in claims 18-19; however, Hashimoto discloses "nucleic acid probes that have a base sequence complementary to the entire or part of a target base sequence (Page 6, Lines 65-67; Page 7, Lines 1-7)".

The Examiner thus concluded that "one of ordinary skill in the art would have been motivated to practice the methods disclosed by Hashimoto (i.e. detection of nucleic acid hybridization through the use of a semiconductive surface) with the semiconductive device disclosed by Cahen because of...the advantage of a safer and more convenient gene detection method that circumvents the use of dangerous (i.e. radioactive) nucleic acid probes. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods".

As applicants have already clarified that the instant application as called for in the independent claims would not have been obvious from Cahen in view of Hashimoto, it follows that all the obviousness rejections under 35 USC 103(a) against claims 5-19 should be withdrawn as well.

Withdrawal of the rejection is in order and is respectfully requested, notwithstanding the commentary in the

rejection relating to the dependent portions of the subsidiary claims.

The prior art documents made of record and not relied upon have been noted, along with the implication that such documents are deemed by the PTO to be insufficiently pertinent to warrant their application against any of applicants' claims.

Applicants have addressed all issues raised in the Official Action in a manner which applicants believe should lead to allowance of the present application. Accordingly, applicants respectfully request favorable reconsideration and allowance.

Respectfully submitted,

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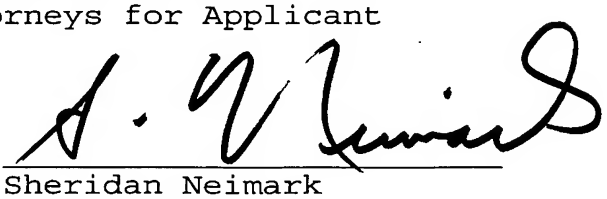
By 
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